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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/534,091	05/06/2005	Juha-Matti Savola	TUR-168	2654

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EXAMINER	
GEMBEH, SHIRLEY V	
ART UNIT	PAPER NUMBER
1628	
MAIL DATE	DELIVERY MODE
12/09/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/534,091	**Applicant(s)** SAVOLA ET AL.	
	Examiner SHIRLEY V. GEMBEH	**Art Unit** 1628	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 17 November 2010 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☐ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires *3* months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *23 and 25-33*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☒ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☒ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

/Brandon J Fetterolf/
Supervisory Patent Examiner, Art Unit 1628

Continuation of 11. does NOT place the application in condition for allowance because: Applicant's argument have been addressed in the office action of record.
Applicant argues that the claimed method requires a specific administration route (absorption via oral mucosa) of fipamezole to a patient. The applicants have discovered a potential side effect (QTc prolongation) is avoided when fipamezole is oromucosally administered. The Patent Office persists in arguing that QTc is associated with heart rate (Official Action, page 4, line 16), despite the contrary testimony of both Dr. Seiler and Dr. Savola. The Examiner now relies on newly-cited Funck-Brentano et al., 83 Circulation 536 (1991) (hereinafter "Funck-Brentano") to support her argument that QTc prolongation or its absence can be predicted from heart rate. Applicant further argues that neither Huupponen et al. or Karjalainen et al. disclose or suggest anything about QTc prolongation or its absence by either atipamezole or fipamezole. In particular, Applicant argues that QTc prolongation cannot be predicted.
In response, the claims are directed to a method of administering a formulation comprising an active ingredient of formula I, comprising oromucosal administration.
Huupponen specifically teaches administering atepamezole (i.e., a compound with the same core structure with the compound of formula I in claim 23 oromucosally) It is therefore reasonable that the claimed compound with the same core structure that differs only by one substituent administered the same way as the claimed subject matter would reasonably have the same QTc effect. The only difference is that Huupponen has hydrogen versus a halogen or hydroxy as claimed. One having ordinary skill in the art would have been motivated to prepare the instantly, claimed compound because such structurally homologous compounds are expected to possess similar properties. It has been held that compounds that are structurally homologous to prior art compounds are prima facie obvious, absent a showing of unexpected results. In re Hass, 60 USPQ 544 (CCPA 1944); In re Henze, 85 USPQ 261 (CCPA 1950). Applicant's argument that Neither Huupponen et al. or Karjalainen et al. disclose or suggest anything about QTc prolongation or its absence by either atipamezole or fipamezole is found not persuasive because QTc prolongation is due to the administering of the drug which will intrinsically occur after the drug is administered, It is a characteristic of the drug and secondly the claims do not recite the characteristics claimed. Applicant's argument that Huupponen fails to teach oral mucosal administration is found not persuasive because Huupponen specifically teach administration in a form of spray oromucosally (see page 506, abstract). Karjalainen teaches the same compound. Therefore one of ordinary skill in the art would have been motivated to substitute the compound of Huupponen with Karjalainen's compound with a reasonable expectation of success.
With regards to the argument that the Patent Office persists in arguing that QTC is associated with heart rate despite the declaration submitted by Dr. Seiler or Dr. Savola was considered and is hereby reiterated.
Applicants Declaration under 37 C.F.R. 1.132 executed by Dr. Seiler supports and provides evidence in his/her opinion that one of ordinary skill in the art would have expected fimpamezole to prolong the QTc interval because the concentration of fimpamezole of orally treated. It must be noted that the Declaration is an opinion being presented presumably to overcome the rejection of record. It is noted in the Declaration that emphasis has been put on "my opinion" and therefore is made without underlying facts to support such a position based on sound reasoning that would persuade those skilled in the art, and thus, is a mere conclusionary statement. Therefore the declaration submitted by Jurg P. Seller under 37 CFR 1.132 filed 12/30/09 is insufficient to overcome the rejection of claims 23, 25-30 and 31-33 based upon the rejection set forth by Huupponen (1995) and Karjalainen et al. (US 5,498,623) or Huupponen (1995) and Karjalainen et al. in view of De Prost (US 6,413,988) as set forth in the last Office action because: the declaration contains specific dosage amounts not recited in the claims. Ex parte Gelles 22 USPQ 2d 1318 (at 1319): "The evidence relied upon also should be reasonably commensurate in scope with the subject matter claimed and illustrate the claimed subject matter "as a class" relative to the prior art subject matter."
Also in order to claim unexpected result Applicant should note that there are three major points that should be considered:
The unexpected result must truly be unexpected, It must be commensurate in scope (show a trend representing the scope) and lastly a direct comparison with the closest prior art of record, which has not been done. As recognized as a class of chemical compounds mean that there is an expectation from the knowledge in the art that members of the class will behave in the same way in the context of the claimed invention. In other words, each member could be substituted one for the other, with the expectation that the same intended result would be achieved.

With regards to the Declaration under Dr. Savola, Declarant opinion is that one of ordinary skill in the art would not assume anything from Huupponen regarding the presence or absence of QTc prolongation upon oromucosal administration of atipamezole.
The QTc value relied upon by Declarant, Again Applicant has failed to show that the result is truly unexpected, commensurate in scope and show a comparison of the instantly claimed with the prior art.

Regarding the Declaration submitted on 11/17/2010 by Funck-Brentano, the Examiner acknowledges and has carefully considered the declaration and has found it persuasive that one of skill in the art can not predict QTc value based on heart rate. However, it is noted that the declaration appears to have been submitted to rebut the Examiner's previous position and does not appear to be submitted in order to over come the obviousness rejection of record. As such, while sufficient to rebut the previous statement, the Examiner recognizes that the Declaration is insufficient to overcome the prior art rejection for the reasons set forth in the prior office action and below. Because Huupponen specifically teach that their compound is administered the same way (oromucosally) as the instantly claimed compound and as stated above Huupponen's compound with the claimed compound have been recognized as a class of chemical compounds mean that there is an expectation from the knowledge in the art that members of the same class will behave in the same way in the context of the claimed invention. In other words, each member could be substituted one for the other, with the expectation that the same intended result would be achieved.

Applicant's arguments have been fully considered but they are not persuasive as discussed above and already made of record
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